Kidney International, Vol. 68, Supplement 97 (2005), pp. S141–S144

Impact of lifestyle on prevalence of kidney disease in Pima Indians in Mexico and the United States

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Impact of lifestyle on prevalence of kidney disease in Pima Indians in Mexico and the United States.

Pima Indians in the United States and Mexico share a common genetic background but have very different lifestyles. Comparisons were made of the frequency of obesity, diabetes, hypertension, and kidney disease in these geographically separated but susceptible populations. Mexican Pimas had higher levels of physical activity, less obesity, and a lower prevalence of diabetes than their US Pima counterparts. Mean blood pressure rose with worsening glucose tolerance, and the prevalence of elevated urinary albumin excretion was higher in patients with diabetes than in those without, regardless of whether they lived in the United States or Mexico. These findings illustrate the importance of lifestyle in the development of diabetes and in the subsequent occurrence of diabetic kidney disease.

El impacto del estilo de vida sobre la prevalencia de diabetes y sus complicaciones renales en Indios Pima de México y Estados Unidos.

Los Indios Pima de Estados Unidos y México comparten antecedentes genéticos pero tienen estilos de vida muy diferentes. Se hicieron comparaciones de la frecuencia de obesidad, diabetes, hipertensión y enfermedad renal en estas dos poblaciones genéticamente susceptibles pero geográficamente separadas. Los Pimas Mexicanos tuvieron mayores niveles de actividad física, menos obesidad y menor prevalencia de diabetes que su contraparte de Estados Unidos. Se observó que la presión sanguínea aumentó a medida que empeoró la tolerancia a la glucosa. La prevalencia de albúmina urinaria elevada, fue mayor en los sujetos con diabetes que en los no-diabéticos, independientemente de ser Pimas de México o Pimas de Estados Unidos. Estos hallazgos muestran la importancia del estilo de vida en el desarrollo de diabetes y de la subsecuente ocurrencia de enfermedad renal.

The Pima Indians are indigenous to the southwestern United States and northern Mexico. Before contact with the Spanish in the 1600s, Pima Indians occupied a geographic area that extended about 400 miles south of the present U.S./Mexico border to 100 miles north of the border in central Arizona, where the Gila and Salt Rivers converge [1]. Today, many Pima Indians in Arizona still live in reservation communities—primarily in either the Salt River Pima-Maricopa Indian Community or the Gila River Indian Community. Those residing in the Gila River Indian Community participate in an ongoing study of diabetes and its complications and have the world's highest reported prevalence of type 2 diabetes, a disease that was largely unknown in these communities only a few decades ago. They also have an extraordinary rate of kidney disease attributable to diabetes [2, 3]. Because major changes in genetic susceptibility to complex diseases do not occur over 2 or 3 generations, the primary explanation for the high rate of diabetes and kidney disease in the U.S. Pima is most likely a major change in lifestyle.

The village of Maycoba and the surrounding area, on the eastern border of the Mexican State of Sonora in the Sierra Madre, is home to another population of Pima Indians. In contrast to their U.S. counterparts, the Mexican Pima are mainly subsistence farmers who use traditional, nonmechanized tools to grow their crops. They have no electricity or running water, and their present lifestyle probably more closely resembles that of the U.S. Pima before contact with European settlers. In this review, we examine the natural course of diabetic kidney disease in the U.S. Pima Indians and the impact of lifestyle differences between the Mexican and U.S. Pima Indians on the frequency of diabetes, hypertension, and kidney disease in these geographically separated but genetically similar populations [4, 5].

SURVEY METHODS

Mexican Pima

In 1994, a census of the village of Maycoba and the surrounding region was conducted to enumerate all residents of the area and establish their ethnicity, dates of birth, and familial relationships [1, 6, 7]. The Mexican

Key words: Arizona Pima Indians, diabetic nephropathy, lifestyle, Mexican Pima Indians, type 2 diabetes mellitus.

Pima population described in this review included 141 individuals ≥20 years of age with full Pima heritage who lived in Maycoba and the surrounding area. Patients were considered full Pima if they reported that both their parents were Pima.

Each patient was invited to participate in a health examination at the research clinic in the village of El Kipor, some 10 km east of Maycoba. Examinations were conducted in the mornings, with patients fasting, and these examinations included measurements of blood pressure, an oral glucose tolerance test after a 75-g oral glucose load, and measures of urine albumin and creatinine concentration.

United States Pima

Data from the Mexican Pima presented in this report were compared with those from published reports of U.S. Pima Indian patients participating in the longitudinal epidemiologic study of type 2 diabetes mellitus in the Gila River Indian Community [1, 2, 8]. The same measurements were made in the Mexican population, and laboratory specimens from both populations were assayed in the National Institute of Diabetes and Digestive and Kidney Diseases laboratory in Phoenix, Arizona.

RESULTS

Course of kidney disease in the U.S. Pima Indians

The natural history of diabetic kidney disease in the U.S. Pima Indians has been studied extensively and is characterized by a number of phases in which albumin or protein excretion increases, and in which glomerular filtration rate increases and subsequently declines [9]. As the disease progresses, characteristic morphologic and histologic changes occur in the kidney, which may eventually lead to kidney failure [10]. Portions of this report have been published in previous reviews on this topic [11–13].

Among U.S. Pima Indians, elevated urinary albumin excretion (albumin-to-creatinine ratio ≥30 mg/g) is common, and its prevalence is strongly associated with the duration of diabetes; the prevalence is 29% in those with diabetes for <5 years and 86% in those with diabetes for ≥20 years. Microalbuminuria (albumin-to-creatinine ratio = 30–299 mg/g) accounts for 82% of the prevalent cases in Pima Indians with <5 years of diabetes but for only 22% in those with diabetes for ≥20 years, which indicates that the frequency of more severe kidney disease is greater in those with diabetes of longer duration [2]. More than half of U.S. Pimas with type 2 diabetes develop clinical proteinuria within 20 years of the diagnosis of diabetes [14], and once proteinuria develops, an irreversible deterioration of kidney function often ensues that eventually leads to end-stage renal disease. The cumulative incidence of end-stage renal disease in Pima Indians with diabetes is 40% after 10 years and 61% after 15 years of proteinuria [15].

Kidney failure from diabetes was a leading cause of death in U.S. Pima Indians, accounting for 23% of the deaths from natural causes among patients with diabetes during the years 1975 to 1984 [16]. In recent years, however, deaths directly attributable to diabetic nephropathy have declined, due in large part to greater access to and improvements in renal replacement therapy, whereas deaths from ischemic heart disease, a competing cause of death that shares many risk factors with diabetic kidney disease, have risen [17, 18]. Indeed, nearly all excess mortality associated with diabetes in this population occurs in people with proteinuria, and the excess deaths are almost entirely due to cardiovascular and kidney disease [19].

Susceptibility to diabetic nephropathy

Susceptibility to diabetic nephropathy is enhanced by factors other than diabetes per se. Aggregation of kidney disease in families [20], a relationship between parental blood pressure and diabetic nephropathy in the offspring [21], and an association between higher prediabetic blood pressure and the occurrence of kidney disease after the onset of diabetes [22] all point to individual differences in susceptibility. Retardation of kidney development, as occurs in people of low birth weight or with exposure to diabetes in utero, also increases the risk of kidney disease [23, 24]. Each of these factors can be identified before the onset of diabetes, and they provide clinicians with the opportunity to intensify measures to prevent diabetes and related kidney disease in those at greatest risk of developing kidney complications.

Family studies in the U.S. Pima Indians offer compelling evidence for genetic transmission of susceptibility to kidney disease. The results of a segregation analyses were most consistent with an autosomal-codominant inheritance of diabetic nephropathy [25], and linkage analysis tentatively identified several chromosome regions that may contain nephropathy-susceptibility loci on chromosomes 3q, 7q, 18q, and 20p [26]. Studies of candidate genes in some of these regions and additional linkage studies of diabetic nephropathy in larger populations are presently underway.

Diabetes-related determinants of diabetic nephropathy

Once diabetes develops, other factors assume greater importance in predicting the development of diabetic nephropathy, and changes in the strength of some associations may occur as kidney disease progresses [15]. In Pima Indians with diabetes, factors associated with the development of elevated urinary albumin excretion include longer duration of diabetes, higher blood pressure, higher serum cholesterol concentration, poorer glycemic

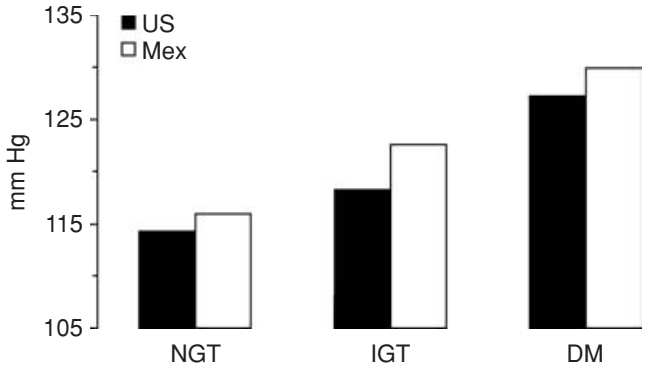

Fig. 1. Mean systolic blood pressure by category of glucose tolerance among Pima Indians living in Maycoba, Mexico (Mex), and in the Gila River Indian Community, Arizona (U.S.). Adapted with permission from Nelson et al [2]. NGT, normal glucose tolerance; IGT, impaired glucose tolerance; DM, type 2 diabetes mellitus.

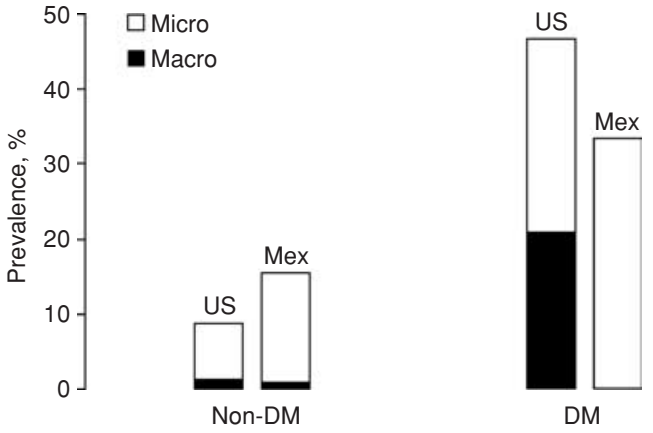

Fig. 2. Prevalence of microalbuminuria (Micro; urinary albumin-to-creatinine ratio of 30–299 mg/g) and macroalbuminuria (Macro; urinary albumin-to-creatinine ratio ≥300 mg/g) among Pima Indians in Maycoba, Mexico (Mex), and in the Gila River Indian Community, Arizona (U.S.). Adapted with permission from Nelson et al [2]. Non-DM, no diabetes mellitus; DM, type 2 diabetes mellitus.

control, lower body mass index, and the presence of diabetic retinopathy [27]. Of these risk factors for nephropathy, duration of diabetes and the levels of blood pressure and glycemic control are most consistently reported in other populations.

Elevated urinary albumin excretion is a risk factor for kidney disease progression, and elevation within the microalbuminuric range in Pima Indians with diabetes is associated with a 10-fold higher risk of progression to proteinuria [28].

Kidney morphology

Kidney biopsy studies in U.S. Pima Indians with diabetes indicate that glomerular volume is greater in more advanced diabetic kidney disease, due principally to expanded mesangial volume. Furthermore, patients with macroalbuminuria have a markedly higher prevalence of global glomerular sclerosis than those with less-advanced kidney disease, and they also have thicker glomerular basement membranes, wider epithelial cell foot processes, and a substantial reduction in the total number of visceral epithelial cells, or podocytes, per glomerulus [10]. Serial kidney biopsy studies in this population suggest this finding is due to loss of podocytes as the diabetic kidney disease progresses [29].

Comparison of U.S. and Mexican Pima Indians

The Mexican Pima Indians are mainly subsistence farmers, and this is reflected in a significantly higher level of physical activity than their U.S. counterparts [7]. In addition, Mexican Pima were shorter, lighter, and had lower body mass indices than the U.S. Pima. Obesity (body mass index ≥30) was 4-fold higher and diabetes 6-fold higher in the U.S. Pima than in their Mexican Pima counterparts [6, 8].

Although the prevalence of diabetes was much lower in the Mexican than in the U.S. Pima, once they developed impaired glucose tolerance or diabetes, the frequency of associated medical conditions increased. In both Mexican and U.S. Pima [2], for example, systolic blood pressure was positively associated with categories of glucose tolerance (Fig. 1). Furthermore, Mexican Pima were not spared kidney complications of diabetes. The prevalence of elevated urinary albumin excretion, assessed by the urinary albumin-to-creatinine ratio, was higher in the diabetic than the nondiabetic Pima Indians in both populations [2] (Fig. 2).

CONCLUSION

Diabetes and kidney disease have both genetic and environmental determinants. Our article examines the course of kidney disease in type 2 diabetes in the U.S. Pima Indians and compares the prevalence of diabetic kidney disease in 2 groups of Pima Indians with contrasting lifestyles. In spite of geographic separation, linguistic studies and genetic distance estimates indicate that these populations share a very similar genetic background [4, 5] and, therefore, in all likelihood, carry a similar burden of diabetes and diabetic kidney disease susceptibility genes. Hence, the major differences in the prevalence of diabetes can only be attributed to differences in environment and lifestyle. Despite the markedly different prevalence of diabetes in the U.S. and Mexican Pima Indians, however, the impact of diabetes on the prevalence of hypertension and elevated urinary albumin excretion was similar in both populations.

These findings illustrate that lifestyle factors are major determinants of diabetes. Once diabetes develops,

however, kidney disease will follow in populations susceptible to this complication. The importance of diabetes prevention in preventing kidney disease in these populations, therefore, cannot be overemphasized. Indeed, our findings suggest that diabetes prevention may be the most effective means of reducing the incidence of diabetic kidney disease worldwide.

ACKNOWLEDGMENTS

We wish to thank the Pima Indians from Maycoba and the Gila River Indian Community for participating in the studies reported in this review. This work was supported in part by grant number National Institutes of Health-DK-49957.

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